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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/634,463	08/04/2003	Robert W. Brueggemeier	22727/04124	6736

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EXAMINER	
CHANG, CELIA C	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 04/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/634,463	BRUEGGEMEIER ET AL.	
	Examiner	Art Unit	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *06 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I, claims 2-8 in the reply filed on Jan. 6, 2005 is acknowledged. The traversal is on the ground that the examiner did not show that examination of the entire application would be a serious burden. This is not found persuasive because it was clearly delineated that the compounds of the claims encompassed separate "class" and subclasses. It is noted that class 546 in the US classification system is drawn to six membered ring compounds with one nitrogen; class 544 in the US classification system is drawn to six membered ring compounds with one nitrogen and at least another heteroatom, class 548 in the US classification system is drawn to five membered ring compounds with one nitrogen, and class 549 in the US classification system is drawn to six membered ring compounds with chacogen (O/S) as the heteroatom. It was clearly demonstrated that the search for each class is not coextensive the search for one group is not required by another group. Applicants were advised that

"Should applicant traverse on the ground that the groups are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the groups to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention."

Applicants provided mere argument without factual evidence or admission that the search was without burden because of art recognized obviousness of all the compounds. Absent of factual support of clearly admission on the record, the serious burden established in the record is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 2-8 and claims 1, 9-19 reading on R3 is piperidine is examined. The remaining compounds of claims 1, 9-19 are withdrawn from consideration per 37 CFR 1.142(b).

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is *presented prior to* final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be **allowable**, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between

product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of In re Ochiai; In re Brouwer and 35 U.S.C.§ 103(b)," 1184 O.G. 86 (March 26, 1996).

Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include all the limitations of the product claims. *Applicants are reminded of propriety of process of use claims in consideration of the "reach-trough" format, which is drawn to mechanistic, receptor binding or enzymatic functionality. Reach through claims are considered lacking of descriptive and enabling support from the specification. Thus, rejoinable process of use claims are those with particular disease named with efficacy support from the specification for treating the particular disease.* **Failure to do so may result in a loss of the right to rejoinder.**

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01. Filing of appropriate terminal disclaimer in anticipation of a rejoinder may speed prosecution and the process of rejoinder.

Claims 20-23 if made dependent on the elected compounds can be rejoined with the compounds in prosecution to the extend of the elected compounds.

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (f) he did not himself invent the subject matter sought to be patented.

Claims 1-23 are rejected under 35 U.S.C. 102(f) as being anticipated by Kim et al. CA 139:117307.

See anticipatory compounds and "different" inventorship with at least one common inventor. Applicants are advised to follow MPEP 2137 for clarification of ambiguity of inventorship created by the article.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claim 1 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chiesi et al. WO 98/29403 in view of King et al. Medicinal chemistry p.206-209.

Determination of the scope and content of the prior art (MPEP §2141.01)

Chiesi et al. '403 disclosed estrogen receptor modulating compounds analogous to the instant claims and two species are found on page 9, tope two compounds.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

The difference between Chiesi et al. '403 species and the instant claims is that instead of X is SO or SO2, the Chiesi et al. '403 species have CO linker. King et al taught that the replacement of a carbonyl group in a known compound with SO or SO2 is the well recognized bioisosteric replacement (see p. 208). Bioisosteric replacement is expected to retain biological activity since such is the design of the replacement (see p. 207).

Finding of prima facie obviousness---rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art in the field of estrogen receptor modulating isoflavonone compound art would be motivated to modify the Chiesi et al. '403 compounds by the bioisosteric replacement i.e. the instant claims, **because** such modification is suggested by medicinal chemists will obtain more lead compound with retained biological activity.

4. Claims 20-21 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide description and enablement for the scope as claimed. The specification lacks description and does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to operate the invention commensurate in scope with these claims.

As stated in the MPEP 2164.01(a) "There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". The factors to be considered herein are those set forth as the In re Wands, 8 USPQ 2nd 1400 (1988) decision.

Nature of invention

The claims are drawn to "treating, inhibiting or delaying on set of a cancer in a subject in need of such treatment comprising administering a therapeutically effective amount of compound of [elected compounds]".

Initially, applicants' attention is drawn to that cancer treatment is highly unpredictable. While certain compounds can treat certain cancer, no one compound has been known to be able to treat all cancer. In the instant case, no description except for efficacy in two breast cancer cell lines, were found as to guide one skilled in the art of how to formula dosage, site selection etc. as to treat any other cancer by the claimed compound. In addition, how can one being diagnosed with cancer be "delayed" on set of cancer?

The state of the art and predictability

Cancer treatment is highly unpredictable, examples of the instant claimed compounds were shown to have proliferation inhibition activity on MCF-7 and MDA-MB-231 two hormone dependent breast cancer cell lines. No nexus can be found that activity in the two hormone dependent breast cancer cell lines can be extrapolated to any other cancer (see NCI cancer screening guidelines p.627-629).

The amount of guidance and working examples

The only description is the efficacy of selected compounds having MCF-7 and MDA-MB-231 hormone dependent breast cancer cell line activity thus are limited to operation in treating or inhibiting proliferation of hormone dependent breast cancer.

5. Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is not understood as to what is the process being claimed by claim 23.

While suppression of proliferation was measured in the two hormone dependent breast cancer cell lines, no information as to what constitutes 'significant binding with estrogen receptors'. It is known that at least the MCF-7 cell line contains estrogen receptor and the suppression of tumor growth is through the mechanism of estrogen receptor modulation for which similar benzopyranyl compounds have been known to operate (see US 6,620,838). It is not clear as to what the scope of the claims is since no description for the "without significantly binding with estrogen receptors" can support the instant scope.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 571-272-0679. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang, can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

OACS/Chang
Apr. 26, 2005-04-26

Celia Chang
Primary Examiner
Art Unit 1625